number of urgency episodes in a 24-hour period, when compared with placebo, was significantly lower with solifenacin 5 mg (−2.85, −51.9%) and 10 mg (−3.07, −54.7%; both $P < .001$), but not with tolterodine (−2.05, −37.9%; $P = .0511$). There was a statistically insignificant decrease in episodes of incontinence with tolterodine (−1.14; $P = .1122$) but a significant decrease in patients treated with solifenacin 5 mg (−1.42; $P = .008$) and 10 mg (−1.45; $P = .0038$). The mean number of voids per 24 hours was significantly lower in patients receiving tolterodine (−1.88, −15%; $P = .0145$), solifenacin 5 mg (−2.19, −17%) and 10 mg (−2.61, −20%; both $P < .001$) than with placebo (−1.20, −8.1%). With all 3 active treatments the mean volume voided/void was significantly higher ($P < .001$).

The use of solifenacin was well tolerated, with dry mouth, mostly mild, the most commonly reported side effect. This was reported in 18.6% of patients receiving tolterodine and in 4.9% receiving placebo, while also reported in 14.0% receiving 5 mg and 21.3% receiving 10 mg solifenacin.

At 5 mg and 10 mg once per day, solifenacin was effective and well tolerated for the treatment of OAB patients with acceptable anticholinergic side effects reported. As is true for all antimuscarinic agents, side-effect profiles with solifenacin should be balanced against efficacy. The low discontinuation rates should provide evidence for clinically meaningful efficacy and tolerability profile. ■

Prostate Cancer

Management of Localized Prostate Cancer

Reviewed by Michael K. Brawer, MD

Northwest Prostate Institute, Northwest Hospital, Seattle, WA

[*Rev Urol.* 2004;6(4):218-219]

The optimum management of clinically localized adenocarcinoma of the prostate remains controversial. The more aggressive approaches involving radical prostatectomy or radiation therapy have generally been applied in the United States. In Western Europe and particularly Scandinavia, watchful waiting has been primarily advocated. A landmark publication by Johansson and colleagues reported in the *Journal of the American Medical Association* in 1997 demonstrated that without initial treatment, only a small proportion of patients actually died from prostate cancer within 15 years of diagnosis.[1]

Natural History of Early, Localized Prostate Cancer

Johansson JE, Andrén O, Andersson SO, et al.

JAMA. 2004;291:2713-2719.

This year, Johansson and colleagues have provided an update of their initial study.[2] The mean follow-up on the initial cohort is now 21 years, and 91% of the patients have died. A total of 223 patients were initially enrolled in this population-based study. Outcome parameters included progression-free, cause-specific, and overall survival. Of the total, 39 men (17%) developed metastatic disease. The authors noted that most patients had a relatively uneventful course during the initial 15 years of monitoring.

However, patients suffered a significant decrease in progression-free survival (from 45% to 36%) with longer follow-up. Metastasis-free survival decreased from 76.9% to 51.2%. Prostate cancer–specific survival also decreased from 78.7% to 54.4%. Perhaps most dramatically, the prostate cancer mortality rate increased from 15 per 1000 person-years during the first 15 years of follow-up to 44 per 1000 person-years in the cohort followed beyond 15 years. The authors concluded, "Although most prostate cancers diagnosed at an early stage have indolent course, local tumor progression and aggressive metastatic disease may develop in the long term. These findings would support early radical treatment, notably among patients with an estimated life expectancy exceeding 15 years."

Clearly, this is an important addition to the prostate cancer literature. The authors are to be commended for continuing to follow their initial cohort.

Several caveats should be noted. At the time of diagnosis, the average age was 72 years, which is older than that at current diagnosis. Thus, the issue of competing mortality is more problematic in the Johansson series. No comparison groups (ie, men treated with surgery or radiation from the initial cohort) are provided. This renders meaningful comparison with those seeking active treatment difficult, at best. The power of a randomized clinical trial cannot be minimized.

Johansson and associates, as well as others, have clearly stated that the only way to compare treatment with expectant management is by randomized clinical trials. A trial in which men were randomized to radical prostatectomy versus watchful waiting conducted in Scandinavia was reported by Holmberg and associates in 2002.[3]

In this study, a 50% reduction in prostate cancer mortality in the arm that underwent radical prostatectomy was noted but there was no difference in overall survival. Unfortunately, prostate-specific antigen (PSA) levels were not used for diagnosis in this study.

Obviously, all of the patients in the initial Johansson cohort were diagnosed prior to the PSA era. This is significant because of the lead time afforded by PSA diagnosis. The answer to the most relevant question remains unknown: Would men who were diagnosed in the PSA era with significant lead time have the same progression 15 years after diagnosis or would this be delayed to more than 25 years after enrolling? Obviously, this cannot be answered in the present study, and we must await the result of the Prostate Intervention versus Observation Trial (PIVOT) to provide insight in this regard.[4] This relatively contemporary US investigation has enrolled the majority of men with T1c cancer diagnosed by an elevated PSA level.

Johansson and associates, as well as others, have clearly stated that the only way to compare treatment with expectant management is by randomized clinical trials.

In conclusion, the Johansson study certainly provides food for thought and will undoubtedly be interpreted as supporting early detection and aggressive management. Caution still needs to be exercised for the reasons noted above, and we anxiously await the US randomized trials. In the meantime, it is incumbent on urologists to describe the risk/benefit ratio carefully to their patients seeking therapy for clinically localized prostate cancer. Clearly, well-informed prostate cancer patients, perhaps more than elsewhere in oncology, will be able to make better treatment decisions. ■

References

1. Johansson JE, Holmberg L, Johansson S, et al. Fifteen-year survival in prostate cancer. A prospective, population-based study in Sweden. *JAMA*. 1997;277:467-471.
2. Johansson JE, Andrén O, Andersson SO, et al. Natural history of early, localized prostate cancer. *JAMA*. 2004;291:2713-2719.
3. Holmberg L, Bill-Axelson A, Helgesen F, et al. A randomized trial comparing radical prostatectomy with watchful waiting in early prostate cancer. *N Engl J Med*. 2002;347:781-789.
4. Wilt TJ, Brawer MK. The Prostate Cancer Intervention versus Observation Trial (PIVOT). *Oncology (Huntingt)*. 1997;11:1133-1143.